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Too Restrictive Exclusion Criteria in Advanced Stage Lung Cancer Therapeutic Trials: Are We Missing the Target?

To the Editor:

With 965,000 new cases worldwide in 2002 in men and 387,000 new cases in women, lung cancer is the most common cancer. Because of its poor prognosis, 1.2×10^6 people died of lung cancer in that year.[1] Though its incidence has stopped increasing, particularly for men, in countries where efficient tobacco control policies have been implemented, its global incidence is still on the rise.[1]

This dramatic situation is due to the high worldwide prevalence of tobacco smoking and the fact that most diagnoses are made at advanced stages when only palliative treatments (chemotherapy ± radiotherapy) can be prescribed, surgery being the only curative treatment.[1]

Obviously, curbing the tobacco pandemic would be an efficient way to prevent lung cancer, but worldwide tobacco smoking is still on the rise, due to the tobacco industry's highly efficient marketing and promotion efforts. Furthermore, even if tobacco smoking were to totally vanish, the lung cancer pandemic would last for a long time since at present, at least in developed countries, nearly one in 2 lung cancers are diagnosed in patients who had already given up smoking.[2]

An efficient early detection procedure has yet to be described for this cancer,[3] therefore, to improve lung cancer prognosis, it is important to try to improve treatment (chemotherapy ± radiotherapy) efficacy. This can only be done through the development of more efficient treatments with the enrollment of patients in clinical trials.

Unfortunately, there are currently very few patients with advanced stage lung cancer (less than 5%) enrolled in clinical trials.[4] For example, in our department, a prospective study of inclusion/noninclusion in clinical trials of patients admitted for stages IIIB and IV nonsmall cell lung cancer (NSCLC) in 2007 showed that, among 217 patients admitted for lung cancer, according to TNM staging, 123 patients with NSCLC (m/f ratio: 96/27; mean age: 61 ± 12 years; 64 adenocarcinoma, 32 squamous cell carcinomas, 2 neuroendocrine carcinomas, 2 large cell carcinomas, 17 undifferentiated carcinomas, and 6 without histology) could have been enrolled in clinical trials open at time of admission. However, only 12 patients (10%) were actually included in a trial. The exclusion criteria were as follows: ± symptomatic brain metastases (n = 29), common comorbidities (Charlson Comorbidity Index-CCI- ≥3) (n = 28), WHO PS ≥ 2 and/or life expectancy <3 months (n = 23), patient refusal or specified requirements (n = 13), technical limitation (tumor biopsy size too small for further molecular analysis, n = 9), patient transferred to another institution (n = 7), lack of organization (n = 2).

Obviously, such a low percentage of included patients is not a representative sample of patients with advanced NSCLC. Low accrual rates have been observed in other clinical settings and several parameters have been suggested to be responsible: age, ethnicity, insurance status, presence of an oncology specialist, etc.[4,5] In the present study, these parameters were not involved since all patients could have been included in clinical trials according to their age, clinical status, TNM staging, acceptance, etc. Our patients were mainly not included because of overly restrictive clinical trial exclusion criteria. As a result, one might question whether the observations resulting from therapeutic protocols based on such restrictive criteria, inevitably leading to biased samples of patients, should be applied to all patients. Thus, it is suggested that, instead of studying a very exclusive subset of patients, future protocols should be targeted toward the main patient population, regardless of clinical status, but for terminally ill patients.

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Zoledronic Acid and Survival in Patients with Metastatic Bone Disease From Lung Cancer and Elevated Markers of Osteoclast Activity: A Novel Molecular Mechanism

To the Editor:

Dear Sir, I read with great interest the paper by Hirsh et al.[1]

Disclosure: The author declares no conflict of interest.
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